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Carcinogenicity of Oil Shale Tars, Some of Their Components, and Commercial Products

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Bioassays for carcinogenicity of various primary processing products (crude oils or tars) and commercial products obtained from Estorian oil shale have been carried out since 1951. The products (undiluted or diluted) were painted twice weekly 50 times on the interscapular area of the skin of random-bred or $CC_{57}Br$ mice. The products processed at high temperatures have a higher carcinogenic activity. Blends of products containing over 10% of high temperature crude oil (chamber furnace oil) have about the same carcinogenic activity as the latter. There is no strict correlation between the concentration of benzo(a)pyrene (BP) in oil shale products and their carcinogenic activity. Determination of BP in such products can serve as an approximate estimate of carcinogenic properties.

The results of animal experiments with chromatographic fractions of the high temperature shale oil demonstrated the presence of compounds which lengthen the latency period of the carcinogenic effect of BP in the aromatic fraction of this oil as well as other carcinogens and compounds enhancing the activity of carcinogenic compounds.

Under industrial conditions, contact of workers with carcinogenic shale oils can be reduced by means of coking the carcinogenic oils, which results in production of solid coke and of distillate which is recycled. Medical vaseline potentiates the carcinogenic action of BP and similar compounds. Dilution of shale oils with oils containing aliphatic hydrocarbons cannot be considered as diminution of the carcinogenic potency of these products.

The main results of animal experiments carried out since 1951 to determine the carcinogenic potency of various primary and commercial products of thermolysis of oil shale from deposits in northeastern Estonia (USSR) will be briefly summarized. Attention will also be drawn to some questions of more general interest, such as the value of determination of benzo(a)pyrene (BP) in such products and the role of solvents.

Previous studies on the carcinogenic action of Scottish oil shale processing products (*1–4*) were familiar to us as were publications on occupational tumors induced by various tars and oils in the Scottish oil shale industry, cotton spinning, and other industries (*5–9*).

The carcinogenic activity of primary oil shale tars from other Soviet oil shale deposits (Veimarn, Gdov) was comparatively weak (*10, 11*). Larionov (*12*) tested some tars obtained from Estonian oil shales and found that only the tar from the chamber oven pilot plant, produced at temperatures up to 1000°C, possesses carcinogenic properties.

In our earlier experiments we used random-bred white mice in skin painting experiments. Undiluted (later also diluted) products were applied twice weekly (50 times) on the interscapular area of the skin. Periodic examinations of skin changes and post mortems with histological investigations of changes in various organs were performed. In most cases the BP concentrations in products under investigation was carried out in the Institute of Chemistry of the Academy of Sciences of the Estonian SSR. The criterion of malignancy was the histological demonstration of penetration of the tumor into the muscular layer.

Table 1 shows the results of experiments with six samples of primary processing products of oil shale which we call tars or crudes; of these, the chamber oven tar is processed at about 1000°C, while the generator, tunnel oven, and solid heat carrier tars are processed at temperatures ranging from 400 to 550°C.

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The effective number of mice is the number alive at the time of appearance of the first tumor. Table 2 presents data on the carcinogenicity of some commercial products. The carcinogenic activity in commercial products containing the highly carcinogenic chamber oven tar is obvious; on the other hand, the carcinogenicity of various samples of chamber oven tar is different, and there is no clear relationship between the proportion of chamber oven tar in complex mixtures and their carcinogenic potency.

Table 3 presents data on carcinogenicity of asphalts produced by three different methods from heavy fractions of low temperature tars. The oxidized (blown) asphalt containing considerably less BP is less carcinogenic than the bottom asphalt obtained as residue of vacuum distillation of these heavy fractions. The cold solvent extraction residue appeared to be even less carcinogenic, in spite of slightly higher BP concentration. The light fraction obtained in the solvent extraction process with approximately similar BP content had a considerably stronger carcinogenicity. Apparently the BP concentration and carcinogenic potency are not completely correlated.

Table 4 shows some results of later experiments by Vinkmann carried out with some commercial products mostly in $CC_{57}Br$ mice. There is a near, but not complete, correlation between the BP concentration and the carcinogenicity of the product. Some tars have been repeatedly tested as their composition was not absolutely constant; the results however are in general similar.

The main conclusion which can be drawn from these tests is that the higher carcinogenic activity occurs in the products processed at high temperature. Even a blend of tars containing over 10% of chamber oven tar has about the same carcinogenic

Table 1. Carcinogenicity of primary processing products of oil shale.

No.	Product	BP, ppm	Initial no. of mice, (random-bred)	Effective no. of mice	Time to first tumor, weeks	No. of mice with skin tumors	No. of mice with malignant skin tumors
1	Chamber oven tar 1	1000	111	88	10	49	27
2	Generator tar	100	105	73	10	21	—
3	Tunnel oven tar	10	70	34	89	12	2
4	SHC tar (intermediate pilot plant)	—	122	68	13	46	4
5	Chamber oven tar 2	1700	122	74	8	15	7
6	Dephenolated chamber oven tar	2000	107	83	10	56	33

Table 2. Carcinogenicity of some secondary oil shale processing products.

No.	Product	Proportion of chamber oven tar, %	Initial no. of mice	Effective no. of mice	Time of first tumor, weeks	No. of mice with skin tumors	No. of mice with malignant skin tumors
1	Fuel oil	15	170	50	10	23	12
2	Impregnating oil	40	100	13	20	9	2
3	Rubber softening oil	—	90	—	—	—	—
4	Printing ink	—	75	—	—	—	—

Table 3. Carcinogenicity of oil shale asphalts.

No.	Product	BP, ppm	Initial no. of mice	Effective no. of mice	Time to first tumor, weeks	No. of mice with skin tumors	No. of mice with malignant skin tumors
1	Bottom asphalt	1000	70[a]	44	10	24	7
2	Blown asphalt	30	70[a]	48	15	12	2
3	Solvent extraction	75	50[b]	30	26	1	—
4	Solvent extraction residue light fraction	85	50[b]	45	12	9	1

[a] Random-bred.
[b] C_{57}B1 strain.

activity as the undiluted chamber oven tar. Oil shale tars, being mixtures of numerous different compounds, contain other carcinogenic compounds in addition to BP. Eĭsen (*13*) determined 0.017% BP, 0.46% various derivatives of BP, 0.3% 1,2-benzo(a) anthracene, and various other polycyclic aromatic hydrocarbons in a sample of chamber oven tar.

We carried out experiments with chromatographic fractions of aromatic compounds of the chamber oven tar containing various amounts of BP in order to ascertain whether these fractions also contain compounds having anti- or cocarcinogenic properties. The fractions were diluted in benzene (3%), and a positive control group was included in which mice were painted with a 0.2% BP solution in benzene. Table 5 shows that the fractions had a different carcinogenic activity which is clearer when the formula of Reissig (*14*) is applied, showing the carcinogenic effect.

$$E_t = 100\ T_t/(A_o - M_t)$$

where $T_t = T^m_t + T^v_t$

Table 4. Carcinogenicity of some newer commercial oil shale products and tars.

No.	Product	BP, ppm	Initial no. of mice	Effective no. of mice	Time to first tumor, weeks	No. of mice with skin tumors	No. of mice with malignant skin tumors
1	Generator tar		68[a]	61	20	10	6
2	Tunnel oven tar		68[a]	66	10	10	2
3	Solid heat carrier (SHC) tar		68[a]	67	12	10	6
4	Solvent		53[a]	—	—	—	—
5	LSP-1 lacquer	500	52[a]	50	10	45	37
6	Diphenyl ketone resin 1:1 (DFK 4) in acetone		50[a]	—	—	—	—
7	DFK-8 1:1 in acetone		48[b]	—	—	—	—
8	N12-K (Tanning reagent) 50% water solution		48[b]	—	—	—	—
9	Generator residue 1:1 in olive oil	10	50[b]	50	10	22	15
10	Polymer residues (from compressors) 1:1 olive oil	8	50[b]	—	—	—	—
11	Tolichton		50[a]	—	—	—	—
12	Gas gasoline pyrolytic tar 40% in solvent	2800	52[a]	50	10	45	37
13	SHC tar, intermediate fraction	20	32[a]	15	22	6	0
14	SHC tar, heavy fraction	30	31[a]	29	10	11	4
15	Nerosin	25	62[a]	49	10	19	7

[a] $CC_{57}Br$ strain.
[b] Random-bred

Table 5. Carcinogenicity of 3% benzene solutions of some aromatic fractions of chamber oven tar (70 paintings, random-bred mice).

No.	Product	BP, ppm	Total BP dose, mg	Initial no. of mice	Effective No. of mice	Time to first tumor, weeks	No. of mice with skin tumors	No. of mice with malignant skin tumors
1	Fraction 4	—		50	48	52	2	—
2	Fraction 5	—		50	48	32	15	7
3	Fraction 6	70	0.193	50	49	32	15	11
4	Fraction 7	2000	5.544	50	48	23	34	24
5	Fraction 8	50	0.139	50	39	32	14	3
6	Fractions 6–4 (1:1)	35	0.096	50	48	32	22	12
7	2% benzene solution of BP	2000	5.544	50	47	12	33	23

and T^m_t, and T^v_t are the numbers of tumor-bearing live and dead mice, respectively, at time t; A_o is the initial number of mice; M_t is the number of dead mice without tumors at time t; E_t is the carcinogenic effect (in percent) i.e., tumor bearing mice related to mice liable to develop tumors at time t.

These fractions were also injected intramuscularly to mice and painted on the skin of rabbits. Some interesting results were obtained including data on remote tumors in lungs and on skin mastocytomas, which have been published elsewhere (*15*). Figure 1 shows the difference in the development of skin tumors in mice, presenting the carcinogenic effect.

Fraction 7 with the same amount of BP as the solution of pure BP in benzene contains probably compounds lengthening the latency period of the carcinogenic effect of BP. Fraction 5 without BP apparently consists of rather active carcinogenic compounds other than BP and fraction 4 containing no BP has a moderately enhancing effect on the action of fraction 6.

We have cooperated in an effort to diminish the contact of workers with the strongly carcinogenic chamber oven tar. Together with Kozhevnikov and Gortalum (*16*) experiments on coking of the chamber oven tar, analyses of BP content of the liquid products involved (initial products and coke distillate), and experiments on the action of the distillate in comparison with the initial tar on mice were carried out.

The initial tar contained 2300 ppm BP, the distillation residue (the immediate material for coking) 6400 ppm, the distillate (after coking), 535 ppm BP. Random-bred mice were painted 50 times (twice weekly) with 15% benzene solutions of the initial tar and the distillate. The results are shown in Table 6.

The distillate has a considerably weaker carcinogenic effect than the initial tar. On the other hand, the concentration of BP again does not correspond to the carcinogenic effect of the products tested. In this way it is possible to diminish the BP concentration by approximately one order of magnitude and what is more important, to convert all highly carcinogenic liquid tars by coking into products less hazardous for workers, as solid coke is less contaminating and the distillate recycled in a closed system. It should be added, that since 1964 a coking department is in operation at the Kohtla-Järve oil shale processing plant, utilizing as a rule the whole amount of produced chamber oven tar.

In the experiments with various fractions of chamber oven tar and in other experiments it appeared repeatedly that the results of quantitative determination of BP do not reflect the actual carcinogenic potency of the products. Such determination can be used only as a rough estimate of carcinogenic properties. To illustrate this we made comparisons by plotting some E_t curves obtained in our experiments.

Figure 2 shows that the dephenolated chamber oven tar, the solution of BP in benzene, and the fraction 7 of the chamber oven tar, all three containing 2000 ppm BP show different degrees of carcinogenic potency, the strongest carcinogenicity was found in the 15 per cent dilution of chamber oven tar in medicinal vaseline containing about ten times less of BP.

Vaseline consists of various aliphatic hydrocarbons. The strong potentiating activity of *n*-dodecane, one representative of such compounds, was clearly demonstrated by Bingham and Falk (*17*).

These results have substantial practical significance, as small amounts of known carcinogenic compounds may under certain circumstances be much more dangerous than could be concluded from their actual concentrations.

Bingham and Falk also discussed the promoting

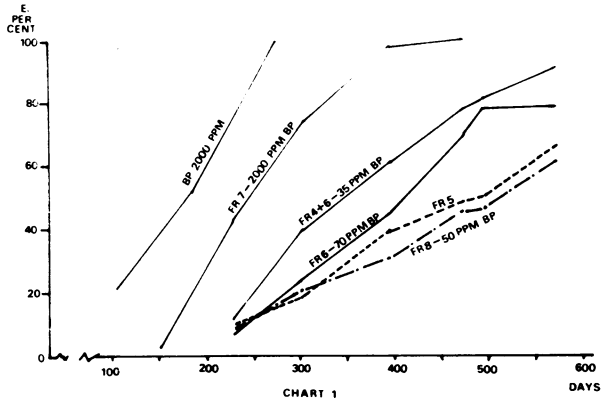

FIGURE 1. Carcinogenic effect of various fractions of chamber oven oil.

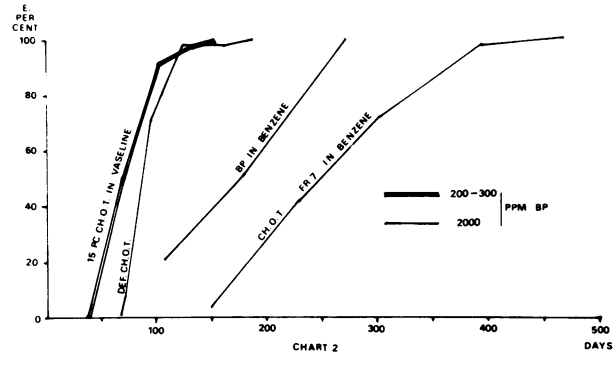

FIGURE 2. Carcinogenic effect of diluted solutions of various fractions of chamber oven oil.

role of phenols (*17*).

Our second paper deals with some data on phenols present in oil shale processing products. From the theoretical point of view as well as from various practical aspects it would appear very important to investigate whether aliphatic hydrocarbons act synergistically with the carcinogen, facilitating its penetration into the cells, or in another way, do they have a phenollike promoting action which can manifest itself after some time has passed, after exposure to the carcinogen. It is necessary to find out whether aliphatic hydrocarbons are active as promoters in the sense of the two-stage scheme of carcinogenicity.

These considerations should be especially taken into account if oil shale processing products should be used as lubricants, cooling mixtures, or cutting oils. This concerns undoubtedly all mineral oils.

An important practical conclusion can be made that dilution of oil shale processing products with "neutral" products, such as refined mineral oils or similar, consisting mainly of aliphatic hydrocarbons, can by no means be considered as diminishing the carcinogenic potency of these products.

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